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| ART UNIT | PAPER NUMBER |
|---|---|
| 1625 | |

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/773,535 | SINGER ET AL. | |
| | Examiner | Art Unit | |
| | Patricia L. Morris | 1625 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 December 2005 and 24 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40 and 42-53* is/are pending in the application.

4a) Of the above claim(s) *1-32,39,40 and 46-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-38 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 33-38 and 42-45 are under consideration in this application.

Claims 1-32, 39, 40 and 46-53 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

### *Election/Restrictions*

The restriction requirement is deemed sound and proper and is hereby maintained.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 33-38 and 42-45 are rejected under 35 U.S.C. 102(a), (b) and/or (e) as being anticpated by Vrecer et al., Kotar et al., Choi et al., Nohara et al., Kato et al and Avrutov et al. I , II for the reasons set forth in the previous Office action.

The declaration under 37 CFR 1.131 filed December 12, 2005 removes the reference of Singer et al. based on applicants' assertion that they constructively reduced the invention to practice prior to August 21, 2002.

Again, Vrecer et al., Kotar et al., Choi et al., Nohara et al.,, Kato et al. and Avrutov I, II specifically disclose the instant compound and compositions. Note, example 1 of Choi et al, examples 2-16 of Singer et al. or claim 7 of Kato et al.. Hence, the instant compound is deemed anticipated therefrom.

Contra to applicants' arguments in the instant response, a novel chemical product is identified first by its "chemical nature", i.e., elemental and atom content. It is a well known fact that many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice. See US Pharmacopis or Muzaffar et al. Thus in the strictest sense, polymorphs are different arrangements and/or different conformations of the **same pure substance** in which the molecules have different arrangements and/or different conformations of the molecules. See Brittain p. 1-2.

Allegations by applications do not take place of objective evidence showing that the alleged "stable" compound is any different from the prior art. See Brittain, page 185.

***Claim Rejections - 35 USC ∋ 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33-38 and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Vcer et al., Kotar et al., Choi et al., Nohara et al.,Kato et al ., and Avrutov et al. I, II in view of Hableblian et al., Chemical & Engineering News, US Pharmacopia, Muzaffar et al, Jain et al., Taday et al, Concise Encyclopedia Chemistry and Brittain et al. (Polymorphism in Pharmaceutical Solids, pages 1-2, 185).

Again, the references teach the stable crystal forms of the instant known compound and as well as the pharmaceutical compositions. Note claim 7 of Kato et al., example 1 of Choi et al. or example 3 of Avrutov et al. II . Habeblian et al., Muzaffar et al., Jain et al. and Taday et al. teach that the compounds exist in different crystalline forms. Chemical & Engineering News, Muzaffar et al., US Pharmacopia and Concise Encyclopedia teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Hence the claimed crystalline form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references. It would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different stable crystalline forms. No unexpected or unobvious properties are noted.

Contra to applicants' assertions in the instant response, one having ordinary skill in the art would find the claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As clearly stated by Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer (CCPA 1966) 354 F2d 664, 148 USPQ 268, ex parte Hartop 139 USPQ 525, that a product which is merely a different form of a known compound, notwithstanding that some desirable results are obtained therefrom, is unpatentable. The instant claims are drawn to the ***same pure substance*** as the prior art that only have *different arrangements and/or different conformations of the molecule*. A mere difference in a physical property is a well known conventional variation for the same pure substance is *prima facie* obvious.

Applicants do not point to any objective evidence which demonstrates that the claimed compound *vis-à-vis* the prior art compound exhibit any properties which are actually different from the closest prior compound embraced by the prior art. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977); In re Hoch, 428 F.2d 1341, 166 USPQ 406 (CCPA 1970). Also, not page 185, lines 4-7, of Brittain et al.

***Claim Rejections - 35 USC ∋ 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-38 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Again, there is a lack of description as to whether the compositions are able to maintain the compound in the stable form claimed. Processing a compound into a pharmaceutical composition could create a different form than the crystalline form being claimed or even back to the compound itself. See pages 912-913 of Habeblian. Doelker et al. Abstract, "One may also observe changes in technology or pharmaceutical properties that are due to polymorphic environmental conditions undergone by the product or dosage form." Taday et al. p 831…Once in the desired crystalline form, the polymorphic form may be changed by incorrect storage or even during tablet preparation" and p. 836, figure 8, wherein the compound form four in the pharmaceutical composition resulted in similar spectra. The specification fails to describe the pharmaceutical compositions claimed in terms of their X-ray diffraction pattern or infrared spectrum data.

Contra to applicants' arguments in the instant response, applicants have **failed to provide any objective evidence that the instant polymorphs are indeed maintained in the compositions.** Chemical & Engineering News disclose that formulation of drugs or pharmaceuticals in its metastable forms, for example, on polymorph, is highly unpredictable. The metastable forms will disappear and change into the most thermodynamically stable form. Muzaffar et al., p. 60 states "At any one temperature and pressure only one crystal form of a drug is stable and any other polymorph existing under these conditions will convert to the stable form." And p. 63-65 (a)-(h) pharmaceutical preparing processes affect polymorphism.

Again ,the specification lacks description of how the pharmaceutical compositions can be prepared in order to maintain the particular compound of a particular form with the particular infrared spectra and X-ray diffraction being claimed. Otsuka et al., p. 852 "..in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process." Disclosure of X-ray diffraction patterns for pharmaceutical compositions comprising the crystalline forms are lacking in the specification. The specification has also not described how all the crystalline forms and compositions being claimed will be maintained and prevented from converting to other forms when used in the treatment of ulcers.

Applicants' allegations in the instant response do not take place of objective evidence. Applicants have provided no objective evidence that the instant stable form will not be identical to the prior art compound because "*when a crystalline solid is dissolved in solvent, the crystalline structure is lost so that different polymorphs of the same substance will show the same absorption spectra as solution*" (see Jain p. 316). Further, in the aqueous phase, *all physical forms are amorphous* (see Ulicky). It is well recognized in the art that for a given crystalline form of a drug, *in absence of explicit* enabling description, in view of the high degree of unpredictability, even if one is in possession of a particular crystalline form, no predictability can be found in such form will prevail in pharmaceutical compositions. See Chemical & Engineering News.

Further, the specification has not described how the crystalline form and compositions being claimed will be maintained and prevented from converting to other forms when used in the treatment of ulcers. In addition, it is well recognized in the art that the compound is given to the

subject in a physiological environment, *i.e.,* administered. As discussed supra, there is no description or enabling support that the instant polymorph will be in its physical form and biological activity results from the particular form instead of the solution state of the compound.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

***The nature of the invention***

The nature of the invention is the preparation of a novel stable forms of the instant compounds and compositions.

***State of the Prior Art***

Polymorphs arise when molecules of a compound stack in the solid state in distinct ways. (See Chemical Engineering News, page 32). Although identical in chemical composition, crystalline forms can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. Additionally, solids may form

solvates. Polymorphs tend to convert from less stable to more stable forms. No method exists to predict the polymorphs of a solid compound with any significant certainty. In drug design, it is best to work with the most stable polymorph, because it will not convert any further, however, the most stable polymorph usually is the least soluble. To improve bioavailability, drug companies sometimes trade off polymorph stability with solubility, choosing to work instead with the less stable forms first, also known as the metastable forms. Polymorphs can convert from one form to another during the manufacturing process of a pharmaceutical drug. See Chemical Engineering News, page 33. This is why it is important to monitor the polymorph during manufacture of the drug to see if it persists during manufacture.

***The amount of direction or guidance and the presence or absence of working examples***

The specification fails to disclose the X-ray diffraction pattern and infrared spectra of the asserted stable compound or compositions containing the stable form. Polymorphs often change into other forms during drug manufacture into a pharmaceutical composition. Based on the unpredictability in the art, the applicant is not entitled to the X-ray diffraction patterns claimed for the compounds and pharmaceutical compositions.

***The breadth of the claims***

The breadth of the claim are drawn to the specific stable form and in addition to the pharmaceutical compositions.

***The quantity of experimentation needed***

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the pharmaceuticals compositions being claimed and verifying that they have the specific X-ray diffraction patterns

being claimed which are not disclosed in the specification. There is also lack of guidance as to whether the instant polymorphs rather than the original compound treats any ulcers.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-38 and 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Again, claims 33-35 are improper product by process claims. Again, original claim 41 demonstrates that applicants are able to describe the instant compound here without resorting to the process. According, claims 33-35 are improper here. Product-by-process claims are not proper in the same application where it has been demonstrated that the compound in question may be described by means of a chemical structure. In re Hughes, 182 USPQ 106 (CCPA 1974). Contra to applicants' arguments in the instant response, applicants are merely claiming a compound well known in the art.

Again., the expression "containing" in claims 42 and 43 is open-ended and allows for the inclusion of other parameters not contemplated by applicants.

Again, the expressions sulfone derivative and sulfide derivatives in claims 42 and 43 are indefinite to their meaning.

Contra to applicants' arguments in the instant response, one cannot tell from a simple reading of the claim what is being claimed. One must first conceive of the alleged sulfones and sulfide derivative. What is meant by derivative? Where is the specific claiming and distinctly pointing out? How can applicants regard as their invention inexact concepts? The breadth of which they could not have possibly checked out with representative exemplification. The expressions are not finite.

Applicants are claiming a compound of the formula. Pure chemistry, a compound. Not a resin of general property ranges, but a pure compound. That compound used for any purpose is taken from the public in a 20-year monopoly to applicants. Then, the public is entitled to know what compound they cannot use. Yet, the claim is not specific to that compound. The public cannot tell what they may not use. How is a claim of the instant breadth defensible in an infringement action?

As applied to pure compounds, In re Cavallito and Gray, 134 USPQ 370, and In re Sus and Schaefer, 134 USPQ 301, are considered to set the proper applicable standard of required definiteness and support.

Claims 33-38 and 42-45 contains the generic name lansoprazole. Where a generic name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the generic name cannot be used properly to identify any particular material or product. A generic name is used to

identify a source of goods, and not the goods themselves. In the present case, the generic name is used to identify/describe a compound have a specific chemical structure and, accordingly, the identification/description is indefinite.

Again, claim 45 lacks antecedent basis for the recited limitations. Contra to applicants assertions in the instant response, there is no basis at all for six months in claim 45.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, AClaims measure invention and resolution of invention must be based on what is claimed.

The C.C.P.A. in 1978 held a that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim. In re Priest, 199 USPQ 11, at 15.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-38 and 42-45 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 29-38 of copending Application No. 10/717,325 in view of view of Haleblian et al., Chemical & Engineering News, US Pharmacopia, Muzaffar et al., Jain et al., Taday et al., Brittain et al. and Concise Encyclopedia Chemistry.

This is a provisional obviousness-type double patenting rejection.

Ser. No 10/717,325 disclose the instant stable compound and compositions The ancillary references teach that the mere existence of further crystalline forms of the compound is not in itself regarded as unexpected. Hence, patentable distinction is not seen.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
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